CDP-CHOLINE & GALANTAMINE IN SCHIZOPHRENIA: A SUSTAINED ALPHA-7 NICOTINIC AGONIST STRATEGY

Submitted by Stephen I. Deutsch, MD, PhD, Nina Schooler, PhD, and Wendy Tenhula, PhD

The activity of certain nerve-cell receptors are reduced in patients with schizophrenia. Dr. Stephen I. Deutsch and his colleagues at the Washington DC VA Medical Center are studying one type of these receptors, the alpha-7 nicotinic acetylcholine receptor, or “alpha-7”. Impaired signaling by this receptor may contribute to the difficulties that many patients with schizophrenia have with filtering and attending to relevant environmental stimuli while ignoring irrelevant signals or “noise” in the environment. These difficulties appear in a very high percentage of patients with schizophrenia and their closely-related biological relatives, including relatives that do not appear to be affected with the illness.

Very recently, the “alpha-7” was identified as a therapeutic “target” in schizophrenia, prompting the development of medication strategies for its long-term stimulation. Ideally, stimulation of this receptor would improve sensory and attention problems seen in schizophrenia. Unfortunately, many drugs that initially stimulate this receptor - so-called agonists - quickly change their pharmacologic effect to block the receptor, and become so-called antagonists. Dr. Deutsch hypothesized that a combination strategy might be needed: using one agent to stimulate the receptor and another to keep the receptor open to that stimulation. CDP-choline, a dietary source of choline, is the agonist agent being used and galantamine, known as a treatment for Alzheimer's Disease, is the medication being used to keep the receptor in its open, responsive state. The VISN 5 MIRECC supported a pilot investigation of this new medication strategy. Specifically, Drs. Stephen I. Deutsch, Barbara L. Schwartz, Nina R. Schooler, and Richard B. Rosse studied the safety, tolerability and therapeutic efficacy of the combination of CDP-choline and galantamine in six schizophrenia patients who were receiving stable doses of anti-psychotic medication but still had prominent residual symptoms. CDP-choline and galantamine were added to the patients’ medication regimens in an open label, 12-week clinical trial. The medication combination was well-tolerated and results were very promising, with individual patients showing improvement of negative symptoms and a decrease in the severity of hallucinations. Three of the six patients requested continuation of the combination at the end of the 12-week trial. An article reporting the results of the pilot study is currently in press.

Based on the results of their pilot study, Dr. Deutsch and colleagues have just received an R34 grant from the National Institute of Mental Health – Interventions to test the alpha-7 nicotinic receptor model in schizophrenia. The study will be known to patients and staff as STAR 1 Schizophrenia Treatment: Agonist Regimens 1.
The "Transforming VHA Mental Health Care: Promoting Recovery and Integrated Care" conference was held from July 17 to July 20, 2007 in Alexandria, VA. This forum combined the Mental Illness Research Education Clinical Center (MIRECC) and Best Practices in Mental Health conferences into one comprehensive mental health conference. The national conference afforded VHA clinicians and researchers the opportunity to learn more about the diverse clinical, research and educational initiatives related to VHA’s Mental Health Strategic Plan, and how the initiatives can be best implemented and monitored in their networks and local medical centers.

The conference was organized around six mental health topics: recovery oriented services, integrated care, promoting access to care and enhancing outcomes, suicide risk identification and prevention, programs for OEF/OIF veterans, and dissemination of evidence-based practices. Innovative research and clinical programs from around the VA addressing these topic areas were presented during breakout sessions. The conference also included several key note speakers. Of note, Ira Katz, MD, Deputy Chief, Patient Care Services, Office for Mental Health, provided an update on the implementation of the VA Mental Health Strategic Plan; Larry Davidson, PhD, and William Anthony, PhD, both presented on recovery oriented mental health services; and Morton Silverman, MD, discussed a public health perspective on suicide risk and prevention. Additionally, the program included an address from the Under Secretary for Health, Brig. Gen. Michael J. Kussman, MD (US Army Ret).

The VISN 5 MIRECC was well represented at the conference. Director Alan S. Bellack, PhD, facilitated the Psychosocial Rehabilitation and Recovery panel sessions, which included a presentation by Lisa Dixon, MD, MPH, on Family Interventions. Drs. Amy Drapalski and Jason Peer presented posters at the MIRECC post-doctoral fellow poster session.

The conference was an efficient and enjoyable way to learn more about the recovery model and how it is being used and implemented across VA Mental Health Services. It was also a great opportunity to meet and network with similarly-minded colleagues from other sites. For more information, all presentations from the conference are available through the VALO website on the VA intranet: http://vaww.sites.lrm.va.gov/vacatalog/cu_detail.asp?id=23001.

WELCOME TO NEW MIRECC STAFF

Melissa Nidecker, PhD, joins the MIRECC as a post-doctoral fellow following the completion of her internship in clinical psychology at the Veterans Affairs Maryland Health Care System/University of Maryland School of Medicine Consortium. Her primary interest is in the area of serious mental illness (SMI) and substance use disorders, with a focus on motivation and behavior change. She also has an interest in substance use disorders in women, which was the topic of both her master's thesis and doctoral dissertation. Dr. Nidecker will be working with Drs. Alan S. Bellack and Melanie Bennett on various research projects related to psychosocial interventions for individuals with dual diagnosis, smoking cessation for those with SMI, and health and treatment issues for women.

If you recognize Melissa's name from several years ago, it's because she worked in Dr. Bellack's Center for the Behavioral Treatment of Schizophrenia as a research assistant. We are delighted to have her back in our research family and know that she will be a great asset to the MIRECC's current projects.
Rebecca (a.k.a. Becky) Pasillas, MA, is assisting Drs. Alan S. Bellack and Richard Goldberg in coordinating efforts related to the Psychosocial Rehabilitation Fellowship Hub Site. She is also assisting Dr. Goldberg with implementing recovery-focused programming and services in the VA. She recently completed her psychology internship at the VAMHCS/UMB Pre-doctoral Psychology Consortium. Becky will return to Reno, Nevada, in September to complete her dissertation and will receive her doctoral degree in clinical psychology from the University of Nevada, Reno, in December 2007.

Suzanne McGarity, MA, joins us at the DC VA as a research assistant for Dr. Wendy Tenhula's study, "The Use of Skills Training to Augment CWT/VI for Veterans with SMI". Suzanne received her Master’s degree in Psychology from Boston University in 2002, and is currently a doctoral candidate in the Clinical Psychology program at American University. She also currently conducts assessments at NIMH, and her clinical work focuses on the behavioral treatment of adults with anxiety disorders.

**UPCOMING EVENTS**

**Family Support and Education Program**
Please watch our website ([http://www.va.gov VISN 5mirecc](http://www.va.gov VISN 5mirecc)) for the September date

The Family Support and Education Program is a monthly program for family members of veterans with serious mental illnesses, including schizophrenia, bipolar disorder, and major depression. The program is designed to help families support veterans' treatment and recovery, as well as assist family members and other caregivers as they cope with the effects of mental illness on the family. Group meetings are held one day a month at the Baltimore VA Medical Center, and involve presentation of information and discussion, which is adapted to the needs of family members and veterans who attend.

To register for the workshop, or for further information, please contact Amy Drapalski, PhD by phone: (410) 605-7000 x4899; or email: amy.drapalski@va.gov.

**Monthly SGA Consultation Seminar**

First Thursday of every month:
September 6, 2007
October 4, 2007
1:00 - 2:00 PM
MIRECC conference room, BVA (6A-168)
or PPVA VTel conference room, Bldg 364
or call 800-767-1750, code 79846

There has been increasing concern, both within and outside of the VA, about the metabolic side effects of second generation antipsychotic medications (SGAs). VAMHCS clinicians are encouraged to bring their difficult or complicated SGA cases to this seminar for consultation and advice. Anyone can present a case or just ask questions in this informal setting, so please join us as we learn from the consultants and from each other. The consultants are Robert Buchanan, MD, from the MIRECC Psychopharmacology
Clinic and Maryland Psychiatric Research Center, and Julie Kreyenbuhl, PhD, PharmD from the MIRECC.

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**Recovery-Oriented Small Grants Program**

**Application Deadline:** September 1, 2007

The VISN 5 MIRECC offers a small grant mechanism to fund recovery-oriented clinical and educational innovations in response to the VA’s Action Agenda to transform VA mental health services to a recovery model. This program especially encourages (but is not limited to) proposals such as: creating, adopting, launching or expanding recovery-oriented clinical or self-help projects, new programs to educate staff, veterans, and/or family members of veterans about mental health recovery models, or specific recovery-oriented services/programs.

For more information, or to receive an application, please contact Alicia Lucksted, PhD, MIRECC Recovery Coordinator, at Alicia.Lucksted@va.gov, 410-605-7451 or 410-706-3244.

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**15th Annual Maryland Schizophrenia Conference**

Tuesday, November 13, 2007
8:00 - 4:30 pm
BWI Airport Marriott
1743 West Nursery Road
Linthicum, MD

On-line registration begins September 3, 2007
Web site: [www.mdschizconf.org](http://www.mdschizconf.org)

VISIT OUR WEBSITE AT
[http://www.va.gov/VISN_5mirecc](http://www.va.gov/VISN_5mirecc)